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Isoxazoles. XXII.[1] A New Synthesis of 4-Isoxazolines and Their Thermal Conversion into Pyrroles[2]

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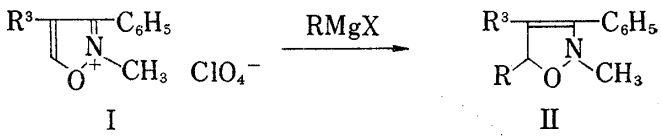
Thirteen N-substituted 4-isoxazoline derivatives were obtained by reaction of 3-unsubstituted and 3,5-disubstituted isoxazolium salts with Grignard reagents. Similarly, 3-benzyl-2-methyl-2,3,4,5-tetrahydronaphth[2,1-*d*]isoxazoles and 3-benzyl-2-ethyl-2,3-dihydrobenzisoxazole were produced by reaction of the corresponding quaternary salts with benzylmagnesium chloride. Thermal reactions of some 4-isoxazoline derivatives and 3-benzyl-2,3,4,5-tetrahydronaphth[2,1-*d*]isoxazole derivatives leading to substituted pyrrole derivatives and 3H-benz[*e*]indole derivatives were investigated. A tentative mechanism for the formation of pyrrole from 4-isoxazoline is also presented.

Among the three types of dihydro derivatives of isoxazoles, 2-isoxazolines have been studied in detail but only recently have a limited number of 4-isoxazolines become available. The latter system has been synthesized mainly by the 1,3-dipolar cycloaddition reaction of nitrones with acetylene carboxylates.[4] Little was known about the 3-isoxazoline system prior to our preceding paper,[5] in which we reported that some 5-unsubstituted isoxazolium salts (I) react with Grignard reagents to give 5-substituted 3-isoxazoline derivatives (II). In a continuation of our studies on isoxazolium salts, the present investigation deals with the synthesis of N-substituted 4-isoxazoline derivatives (IV) from 5-substituted isoxazole quaternary salts (III), and with the thermal conversion of some 4-isoxazolines into pyrrole derivatives (XV).



I II

Chart 1

Reaction of 5-Substituted Isoxazolium Salts (III) with Grignard Reagents

Reaction of 2,4-dimethyl-5-phenylisoxazolium perchlorate (IIIa)[6] with methylmagnesium iodide in ether at 0° yielded an oily product, which was fractionated by chromatography through alumina. An oil of molecular formula $C_{12}H_{15}ON$ (IVa) and a crystalline solid (Va), having the same molecular formula as IVa, were isolated in 41.4 and 21.3% yields, respectively. Similar reaction of 2,3-dimethyl-5-phenylisoxazolium perchlorate (IIIb) with methylmagnesium iodide in ether at low temperature yielded an oil of molecular formula $C_{12}H_{15}ON$ (IVb) in 27.9% yield, together with a small amount of crystalline solid (Vb) of the same molecular formula as IVb. The structures of the oily products, IVa and IVb, were assigned as 2,3,4-trimethyl-5-phenyl- and 2,3,3-trimethyl-5-phenyl-4-isoxazolines, respectively, by the spectral data shown in Table II. Further evidence for the assigned structures was obtained

1) Part XXI: I. Adachi, *Chem. Pharm. Bull.* (Tokyo), **17**, 2209 (1969).
2) For the preliminary communication see: I. Adachi, K. Harada and H. Kanō, *Tetrahedron Letters*, **1969**, 4875.
3) Location: *Fukushima-ku, Osaka, 553, Japan.*
4) R. Huisgen and H. Seidl, *Tetrahedron Letters*, **1963**, 2019; H. Seidl, R. Huisgen and R. Knorr, *Chem. Ber.*, **102**, 904 (1969).
5) I. Adachi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **17**, 2201 (1969).
6) R.B. Woodward and R.A. Olofson, *Tetrahedron*, Suppl., **7**, 415 (1966).

by catalytic reduction with Raney nickel, on which IVa gave a mixture of α-ethylidenepropiophenone (VIa)[7] and α-ethylpropiophenone (VII), and IVb gave isopropylideneacetophenone (VIb).[8] The products Va and Vb were characterized as 2-benzoyl-3-methylamino-2-butene and 1-benzoyl-2-ethylamino-1-propene, respectively, by the analytical and spectral data given in experimental part, and by conversion with hydrazine hydrate into 3,4-dimethyl-5-phenylpyrazole (VIIIa)[9] and 3-methyl-5-phenylpyrazole (VIIIb),[10] respectively. The forma-

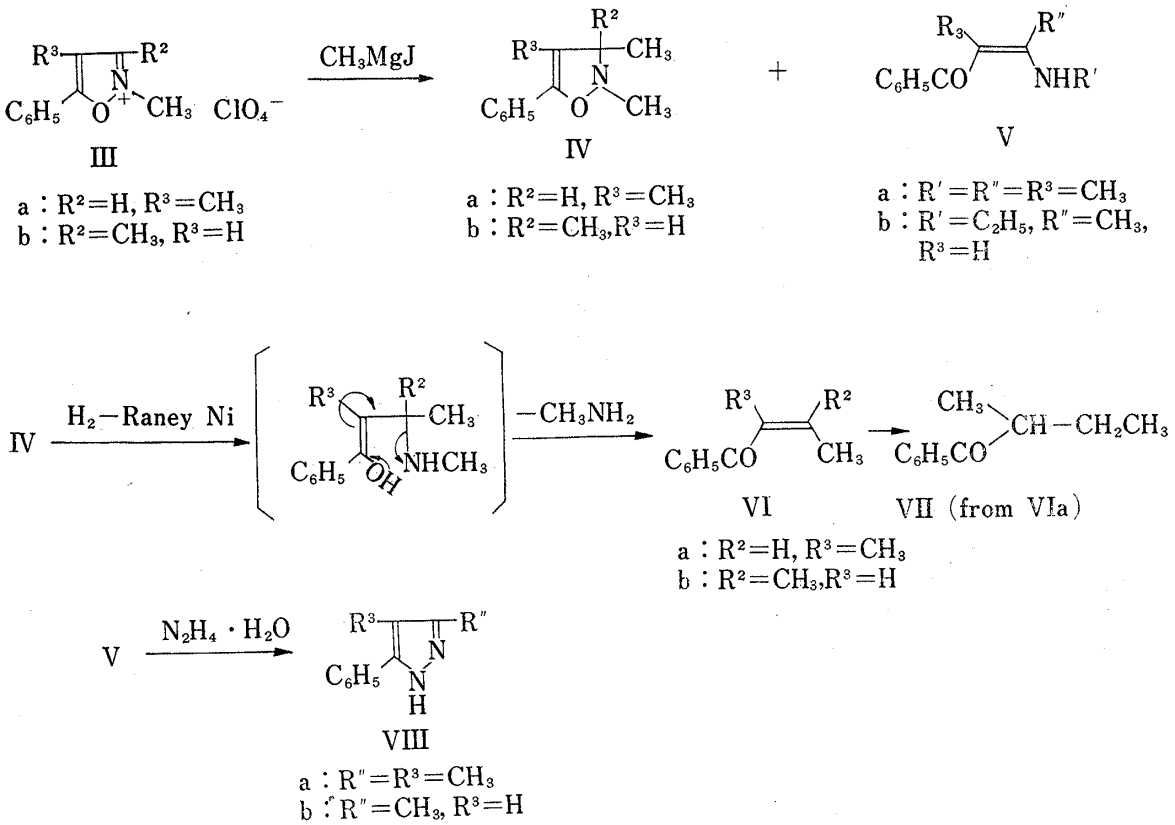


Chart 2

tion of IV and V from III can be rationalized by a mechanism involving two competitive pathways, summarized as courses a and b in Chart 3. Nucleophilic addition of methyl anion at C-3 of III gives IV (course a). On the other hand, initial abstraction by base of the proton at C-3 of IIIa, followed by cleavage of the N-O bond may produce β-oxoketenimine (X), which reacts with methylmagnesium iodide to give Va (course b).[11] In the case of IIIb, which does not retain the proton at C-3 of isoxazole ring, an ylide (IXb) may form by abstraction of the N-methyl proton with base, and then rearranges to a ring-open intermediate (XI), which undergoes methylation to give Vb (course b′).[12]

Similarly, reactions of 2-methyl-5-phenylisoxazolium perchlorate (IIIc) with methyl-, ethyl- and phenylmagnesium halides yielded the corresponding 4-isoxazoline derivatives (IVc—e), together with the ring-cleaved products (Vc—e) (Table I). The reactions of N-

7) E.E. Blaise and I. Herman, *Ann. Chim. Phys.*, **23**, 529 (1911).
8) E.P. Kohler, *Am. Chem. J.*, **42**, 398 (1909).
9) J. Elguero and R. Jacquier, *Bull. Soc. Chim. France*, **1966**, 2832.
10) B. Sjollema, *Liebigs Ann.*, **279**, 248 (1894).
11) Analogous ring-cleavage reaction of 3-unsubstituted isoxazolium salts with base have been reported by Woodward, *et al.*: see Ref. 6.
12) Analogous reaction has been reported by King, *et al.*: see J.F. King and T. Durst, *Can. J. Chem.*, **40**, 882 (1962).

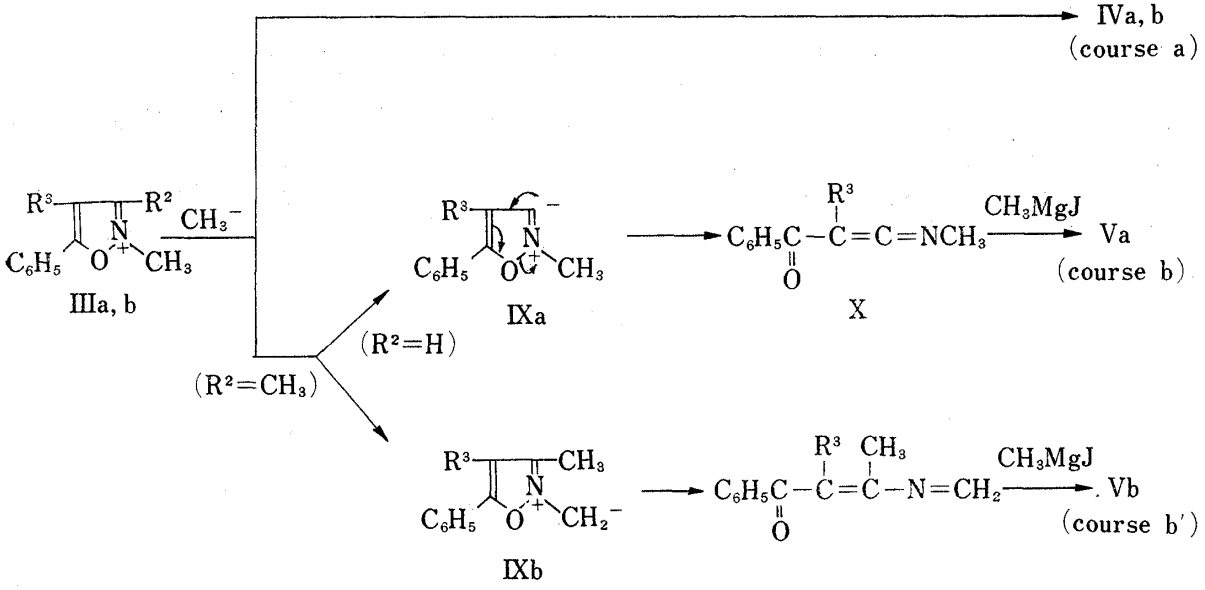


Chart 3

methyl- and N-phenylisoxazolium perchlorates (IIIa—e) with benzyl-, *p*-methylbenzyl-, *p*-chlorobenzyl- and allylmagnesium chlorides yielded only the corresponding 4-isoxazoline derivatives (IVf—m) listed in Table I, and the ring-cleaved products (Vf—m) were not isolated, because of either exclusive addition reaction of the nucleophile to give IV (course a in Chart 3) or instability of the products (V). The analytical and spectral data of the products obtained were all in accord with the assigned structures (see Table II). Reaction of 2-methyl- and 2,3-dimethyl-4,5-dihydronaphth[2,1-*d*]isoxazolium perchlorates (IIIf and g) with benzyl-

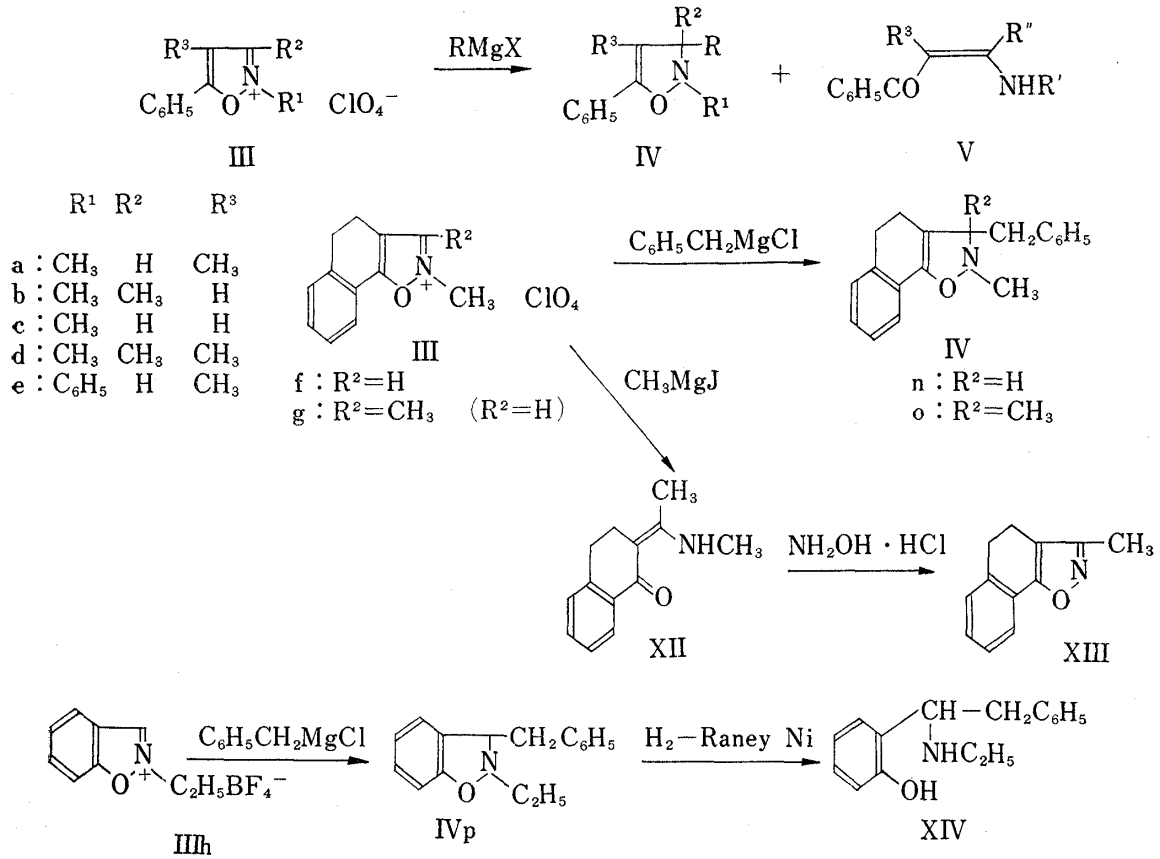
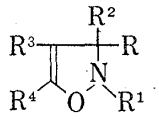
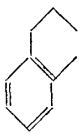
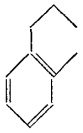


Chart 4

magnesium chloride yielded 3-benzyl-2-methyl- and 3-benzyl-2,3-dimethyl-2,3,4,5-tetrahydronaphth[2,1-*d*]isoxazoles (IVn and o), respectively. Similar reaction of IIIf with methylmagnesium iodide, however, yielded 2-(α-methylamino-ethylidene)-1-tetralone (XII) as the main product, formed through a pathway analogous to course b in Chart 3. Treatment of XII with hydroxylamine hydrochloride in ethanol gave 3-methyl-4,5-dihydronaphth[2,1-*d*]-isoxazole (XIII). The structures of the products (IVn, o and XII) were evidenced by the analytical and spectral data, shown in Tables I and II and in the experimental part, respec-

Table I. 4-Isoxazoline Derivatives (IV)



No.[a]	R	R^1	R^2	R^3	R^4	Yield (%)	Yield (%) of V	Formula	Analysis (%) Calcd. (Found) C	H	N
IVa	CH_3	CH_3	H	CH_3	C_6H_5	41.4	21.3	$C_{12}H_{15}ON$	76.15 (76.44)	7.99 (7.77)	7.40 (6.69)
IVb	CH_3	CH_3	CH_3	H	C_6H_5	21.8	2.0	$C_{12}H_{15}ON$	76.15 (75.59)	7.99 (8.00)	7.40 (7.31)
IVc	CH_3	CH_3	H	H	C_6H_5	9.7	55.0	$C_{11}H_{13}ON$	75.40 (75.03)	7.48 (7.21)	7.99 (7.65)
IVd	C_2H_5	CH_3	H	H	C_6H_5	14.9	75.2	$C_{12}H_{15}ON$	76.15 (76.02)	7.99 (7.81)	7.40 (6.88)
IVe	C_6H_5	CH_3	H	H	C_6H_5	56.9	29.5	$C_{16}H_{15}ON$	80.98 (81.05)	6.37 (6.49)	5.90 (5.81)
IVf	$CH_2C_6H_5$	CH_3	H	H	C_6H_5	95.5	—	$C_{17}H_{17}ON$	81.24 (81.48)	6.82 (6.83)	5.57 (5.26)
IVg	$CH_2C_6H_4$ (*p*-CH_3)	CH_3	H	H	C_6H_5	65.9	—	$C_{18}H_{19}ON$	81.47 (80.99)	7.22 (7.19)	5.28 (5.04)
IVh	$CH_2C_6H_4$ (*p*-Cl)	CH_3	H	H	C_6H_5	98.4	—	$C_{17}H_{16}ONCl$	71.45 (71.80)	5.64 (5.72)	4.90 (4.88)
IVi	$CH_2CH{=}CH_2$	CH_3	H	H	C_6H_5	85.0	—	$C_{13}H_{15}ON$	77.58 (76.85)	7.51 (7.50)	6.96 (6.96)
IVj	$CH_2C_6H_5$	CH_3	H	CH_3	C_6H_5	81.2	—	$C_{18}H_{19}ON$	81.47 (81.29)	7.22 (7.15)	5.28 (5.03)
IVk	$CH_2C_6H_5$	C_6H_5	H	CH_3	C_6H_5	64.1	—	$C_{23}H_{21}ON$	84.37 (84.35)	6.47 (6.32)	4.28 (4.29)
IVl	$CH_2C_6H_5$	CH_3	CH_3	H	C_6H_5	59.8	—	$C_{18}H_{19}ON$	81.47 (81.27)	7.22 (7.26)	5.28 (5.13)
IVm	$CH_2C_6H_5$	CH_3	CH_3	CH_3	C_6H_5	91.0	—	$C_{19}H_{21}ON$	81.68 (81.60)	7.58 (7.64)	5.01 (4.90)
IVn	$CH_2C_6H_5$	CH_3	H			72.9	—	$C_{19}H_{19}ON$	82.28 (82.12)	6.91 (6.95)	5.05 (4.83)
IVo	$CH_2C_6H_5$	CH_3	CH_3			52.0	—	$C_{20}H_{21}ON$	82.44 (82.61)	7.26 (7.33)	4.81 (4.68)
IVp	$CH_2C_6H_5$	C_2H_5	H			67.0	—	$C_{16}H_{17}ON$	80.30 (80.36)	7.16 (7.26)	5.85 (5.84)

a) IVe: mp 67—68° (from EtOH); IVh: mp 76—77° (from hexane); IVk: mp 116—117° (from EtOH); the others were all oily products, which, because of their instability, were purified only by chromatography through alumina.

tively. Reaction of 2-ethylbenzisoxazolium fluoborate (IIIh)[13] with benzylmagnesium chloride yielded 3-benzyl-2-ethyl-2,3-dihydrobenzisoxazole (IVp). Structural assignment for IVp followed from its analytical and spectral data, and from its reductive ring-cleavage with Raney nickel to give *o*-(α-ethylaminophenethyl)phenol (XIV), which was identical with an authentic sample prepared from salicylaldehyde-ethylimide and benzylmagnesium chloride.

TABLE II. Spectral Assignments for 4-Isoxazolines (IV)

No.	$\nu_{C=C}^{Neat}$ cm^{-1}	λ_{max}^{EtOH} nm (log ε)	τ (multiplicity,[a] J=Hz) in $CDCl_3$ (60 MHz)		
			C_3-H or -CH_3	C_4-H or -CH_3	N-CH_3
IVa	1681	224(3.95), 275(3.79)	6.34(qq, 6.2, 1.1)	8.14(d, 1.1)	7.23(s)
IVb	1649	226(4.08), 275(3.85)	8.70(s)	4.83(s)	7.27(s)
IVc	1649	226(3.96), 275(3.83)	6.17(qd, 6.2, 2.4)	4.81(d, 2.4)	7.22(s)
IVd	1682	226(3.92), 275(3.80)	6.34(td, 6.5, 2.7)	4.77(d, 2.7)	7.18(s)
IVe	1649		5.18(d, 2.4)	4.68(d, 2.4)	7.05(s)
IVf	1649	222(4.17), 279(3.90)	6.07(td, 7.0, 2.4)	4.87(d, 2.4)	7.29(s)
IVg	1646	223(4.16), 276(3.88)	6.07(td, 7.0, 2.4)	4.85(d, 2.4)	7.27(s)
IVh	1646	223(4.34), 276(3.97)	6.08(td, 6.6, 2.8)	4.86(d, 2.8)	7.28(s)
IVi	1649	223(4.12), 276(3.91)	6.22(td, 6.6, 2.5)		7.21(s)
IVj	1670	222(4.31), 279(3.88)	6.24(m)	8.18(d, 1.1)	7.37(s)
IVk	1671	240(4.40)	6.88—7.82(m, 3H)	8.63(s)	[b]
IVl	1649	225(4.31), 278(3.99)	8.80(s)	4.90(s)	7.28(s)
IVm	1677	225(sh), 278(3.84)	8.83(s)	8.32(s)	7.42(s)
IVn	1682		6.12(t, 6.4)	6.95—7.98(m, 6H)	7.32(s)
IVp		284(3.52)	5.66(t, 7.0)	[c]	

a) abbreviations used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet *b*) τ 2.52 (m, $3C_6H_5$)
c) τ 6.69—7.53 (m, 4H), 8.89 (t, 7.0, 3H), 2.99 (m, 9H)

Thermal-reactions of Some 4-Isoxazolines (IV)

Heating a solution of 3-benzyl-2-methyl-5-phenyl-4-isoxazoline (IVf) in xylene under reflux for 2.5 hr resulted in the formation of a brown resinous product, from which a crystalline solid of molecular formula $C_{17}H_{15}N$ (XVa) was isolated in 59.0% yield. The ultraviolet (UV) spectrum of the product (XVa) showed maxima at 244 nm (log ε 4.34) and 265 nm

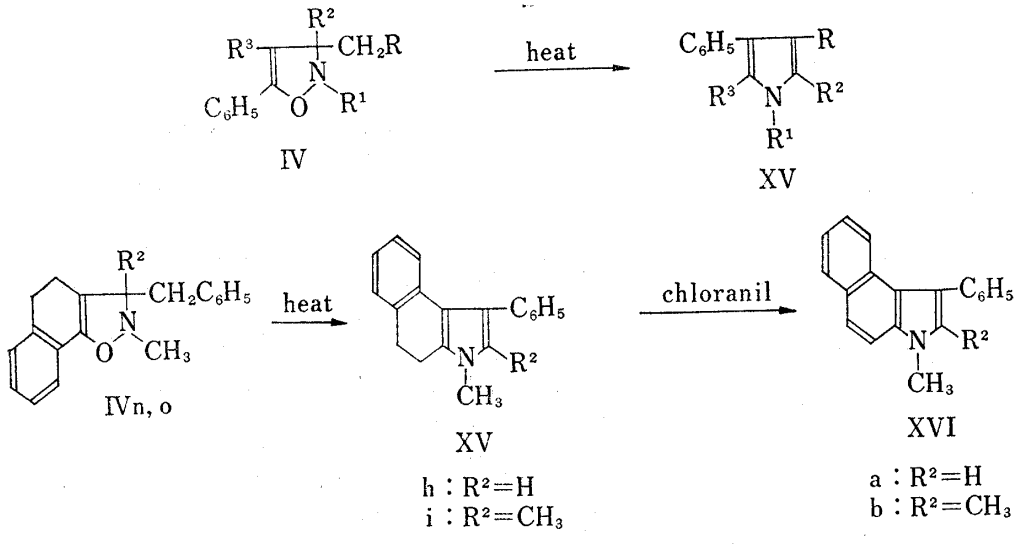
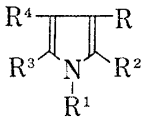


Chart 5

13) D.S. Kemp and R.B. Woodward, *Tetrahedron*, **21**, 3019 (1965).

(sh), and the nuclear magnetic resonance (NMR) spectrum in deuteriochloroform exhibited a singlet at τ 6.47 (methyl hydrogens) and a singlet at τ 3.39 (two aromatic hydrogens) besides a multiplet centered at τ 2.84 (two phenyl groups). These spectral data indicate that the product is 3,4-diphenyl-1-methylpyrrole, and this was confirmed by comparison with an authentic sample obtained by reaction of diethyl N-methyliminodiacetate with benzil.

TABLE III. Pyrrole Derivatives (XVa—g) and 3H-Benz[*e*]indole Derivatives (XVh, i, XVIa, b)



No.	R	R^1	R^2	R^3	R^4	Starting material (IV)	Yield (%)	mp (°C)[a]	Formula	Analysis (%) Calcd. (Found) C	H	N
XVa	C_6H_5	CH_3	H	H	C_6H_5	IVf	59.0	127—128	$C_{17}H_{15}N$	87.51 (87.43)	6.48 (6.47)	6.00 (5.93)
XVb	C_6H_4 (p-CH_3)	CH_3	H	H	C_6H_5	IVg	67.0	88— 90	$C_{18}H_{17}N$	87.41 (87.59)	6.93 (7.01)	5.66 (5.87)
XVc	C_6H_4 (p-Cl)	CH_3	H	H	C_6H_5	IVh	74.1	135—137	$C_{17}H_{14}NCl$	76.26 (76.44)	5.27 (5.24)	5.23 (5.27)
XVd	C_6H_5	CH_3	H	CH_3	C_6H_5	IVj	60.6	92— 93	$C_{18}H_{17}N$	87.41 (87.29)	6.93 (6.96)	5.66 (5.49)
	C_6H_5	CH_3	CH_3	H	C_6H_5	IVl	64.0					
XVe	C_6H_5	CH_3	CH_3	CH_3	C_6H_5	IVm	61.0	143—144	$C_{19}H_{19}N$	87.31 (87.30)	7.33 (7.42)	5.36 (5.18)
XVf	H	CH_3	CH_3	H	C_6H_5	IVb	51.4	48— 49	$C_{12}H_{13}N$	84.17 (84.09)	7.65 (7.12)	8.18 (7.83)
XVg	C_6H_5	C_6H_5	H	CH_3	C_6H_5	IVk	32.3	163—164	$C_{23}H_{19}N$	89.28 (89.48)	6.19 (6.19)	4.53 (4.55)
XVh	C_6H_5	CH_3	H			IVn	58.4	129—130	$C_{19}H_{17}N$	87.99 (88.17)	6.61 (6.45)	5.40 (5.64)
XVi	C_6H_5	CH_3	CH_3			IVo	75.0	119—120	$C_{20}H_{19}N$	87.87 (87.66)	7.01 (7.18)	5.12 (5.25)
XVIa	C_6H_5	CH_3	H				87.2[b]	114—115	$C_{19}H_{15}N$	88.68 (88.74)	5.88 (5.91)	5.44 (5.35)
XVIb	C_6H_5	CH_3	CH_3				70.6[c]	110—111	$C_{19}H_{17}N$	88.52 (88.35)	6.32 (6.60)	5.16 (5.42)

a) Recryst. solvent=MeOH b) Calcd. on the basis of XVh c) Calcd. from XVi

TABLE IV. Spectral Data for Pyrroles (XV) and Benz[*e*]indoles (XVh, i, XVIa, b)

No.	λ_{max}^{EtOH} nm (log ε)	τ (multiplicity, J=Hz) in $CDCl_3$ (60MHz)
XVa	244(4.34), 265(sh)	6.47(s, 3H), 3.39(s, 2H), 2.84(m, 10H)
XVb	244(4.35), 264(sh)	7.70(s, 3H), 6.37(s, 3H), 3.35(s, 2H), 2.87(m, 9H)
XVc	247(4.34), 271(sh)	6.38(s, 3H), 3.35(s, 2H), 2.83(m, 9H)
XVd	244(4.31), 266(sh)	7.88(s, 3H), 6.60(s, 3H), 3.37(s, 1H), 2.89(m, 10H)
XVe	244(4.25), 265(sh)	7.74(s, 6H), 6.52(s, 3H), 2.90(m, 10H)
XVf	235(4.35), 278(sh)	7.78(d, 1.1, 3H), 6.48(s, 3H), 3.81(m, 1H), 3.18(d, 2.2, 1H), 2.74(m, 5H)
XVg	257(4.54)	7.81, (s, 3H)3.04(s, 1H), 2.69(m, 15H)
XVh	246(4.23), 285(4.09)	7.14(m, 4H), 6.45(s, 3H), 3.47(s, 1H), 2.82(m, 9H)
XVi		7.84(s, 3H), 7.12(m, 4H), 6.52(s, 3H), 3.39(m, 9H)
XVIa	224(4.65), 261(4.40), 314(3.97)	6.18(s, 3H), 3.03(s, 1H), 2.32(m, 11H)
XVIb	227(4.61), 259(4.40), 323(4.01)	

Similarly, the substituted pyrrole derivatives (XVb—g) listed in Table III were obtained from the corresponding 4-isoxazoline derivatives. The analytical and spectral data of the products obtained are all in accord with the structures assigned (see Table III and IV). Similar reaction of 3-benzyl-2,3,4,5-tetrahydronaphth[2,1-*d*]isoxazole derivatives (IVn and IVo) yielded the corresponding 1-phenyl-4,5-dihydro-3H-benz[*e*]indoles (XVh and XVi), dehydrogenation of which gave 1-phenyl-3H-benz[*e*]indole derivatives (XVIa and XVIb), respectively. The structural assignments for the products were made from their analytical and spectral data, and by an unequivocal synthesis of XVIa from N-methyl-β-naphthylamine with phenylglyoxal.[14] On the other hand, the expected thermal-conversion of 3-benzyl-2-ethyl-2,3-dihydrobenzisoxazole (IVp) into the corresponding indole derivative did not occur.

A plausible mechanism for the formation of XV from IV is given as follows:

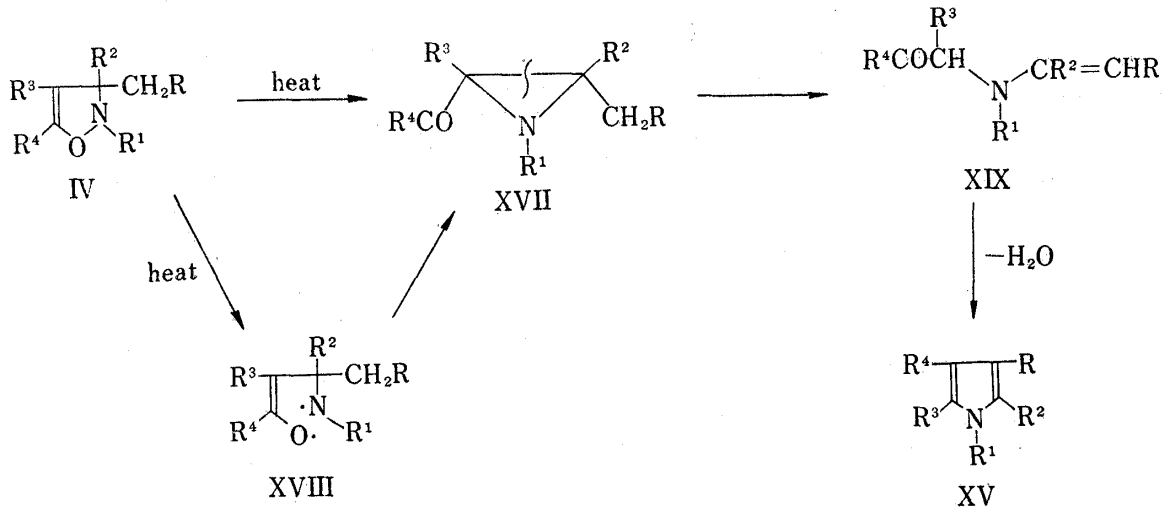


Chart 6

The thermal valence-rearrangement of IV to the 2-acylaziridine (XVII) may involve either a one-step concerted process or initial homolysis of IV into a biradical (XVIII) followed by recombination.[15] The intermediate (XVII) would undergo cleavage of the C-C bond to give the aminoketone (XIX), dehydrative ring closure of which would give the final product (XV).

An analogous thermal rearrangement of some 4-isoxazolines to 2-acylaziridines has been described by Baldwin, *et al.*[16] However, their final products are the corresponding 4-oxazolines. Only two examples of pyrrole formation similar to our present finding have been reported by Acheson, *et al.*,[17] and by Winterfeldt, *et al.*[18]

Experimental

Melting points are uncorrected. The IR spectra were recorded for nujol mulls in the case of solids, or for thin films in the case of liquids, using a JASCO DS-402G spectrophotometer. The UV spectra were recorded in EtOH on a Hitachi EPS-2 spectrophotometer and the NMR spectra were measured with a Varian A-60 analytical NMR spectrometer in $CDCl_3$ with TMS as an internal standard. Solvents and reagents were purified by conventional methods. All extracts were dried over anhydrous magnesium sulfate and evaporated under reduced pressure.

14) The procedure was a modification of Pshorr's method: see R. Pshorr and W. Karo, *Chem. Ber.*, **39**, 3142 (1906).
15) This seems less likely since the rate and products of the reaction were not influenced by oxygen.
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Quaternary Salts (III)——2,4-Dimethyl-5-phenyl- and 2-methyl-5-phenylisoxazolium perchlorates (IIIa and IIIc),[6] 4-Methyl-2,5-diphenylisoxazolium perchlorate (IIIe),[19] and 2-ethylbenzisoxazolium fluoborate (IIIh)[13] were prepared by using the literature methods, respectively. 2,3-Dimethyl-5-phenylisoxazolium perchlorate (IIIb) was prepared by using the following procedure. A mixture of 3-methyl-5-phenylisoxazole[20] (0.01 mole) and dimethyl sulfate (0.011 mole) was first heated at 60° for 0.5 hr, then at 80° over a period of 2 hr, and finally at 110° for 1 hr. After cooling, the mixture was added to a solution of $NaClO_4$ (2.0 g) in H_2O (20 ml). The precipitated perchlorate (IIIb) was collected by filtration. Recrystallization from EtOH gave colorless needles (85.7% yield), mp 188—189°. *Anal.* Calcd. for $C_{11}H_{12}O_5NCl$: C, 48.28; H, 4.42; N, 5.12. Found: C, 48.30; H, 4.55; N, 5.12. 2,3,4-Trimethyl-5-phenylisoxazolium perchlorate (IIId) was prepared from 3,4-dimethyl-5-phenylisoxazole by the similar procedure as the above. Colorless needles (77.5% yield), mp 137—138°. *Anal.* Calcd. for $C_{12}H_{14}O_5NCl$: C, 50.10; H, 4.91; N, 4.87. Found: C, 50.08; H, 4.87; N, 4.77. 2-Methyl-4,5-dihydronaphth[2,1-*d*]isoxazolium perchlorate (IIIf) was prepared from 4,5-dihydronaphth[2,1-*d*]isoxazole[21] by the similar procedure as the above. Colorless needles (33.9% yield), mp 138—139°. *Anal.* Calcd. for $C_{12}H_{12}O_5NCl$: C, 50.45; H, 4.23; N, 5.00. Found: C, 50.42; H, 4.27; N, 5.00. 2,3-Dimethyl-4,5-dihydronaphth[2,1-*d*]isoxazolium perchlorate (IIIg) was prepared from XIII by the similar procedure as the above. Colorless needles (70.4% yield), mp 175—176°. *Anal.* Calcd. for $C_{13}H_{14}O_5NCl$: C, 52.17; H, 4.68; N, 4.68. Found. C, 52.35; H, 4.70; N, 4.40.

Reactions of Quaternary Salts (IIIa—h) with Grignard Reagents——The reactions were carried out by the following procedure. To a solution of RMgX in ether (25 ml), freshly prepared from Mg (0.49 g) and RX (0.02 mole) in ether by the general procedure,[22] was added portionwise quaternary salt (III, 0.01 mole) with stirring and cooling at 0° under an atmosphere of nitrogen and then mixture was stirred at 0° for 2 hr. After addition of NH_4Cl (5 g) in H_2O (40 ml), the mixture was extracted with ether. Evaporation of the solvent left an oily residue, which was chromatographed on alumina with light petroleum followed by C_6H_6. The products (IV) listed in Table I were isolated, together with the following ring-cleavage products (V, XII), respectively.

2-Benzoyl-3-methylamino-2-butene (Va), mp 70—71° (from hexane); ν_{max}^{Nujol} 1591, 1538 cm^{-1} (–CO>=<NH–); τ in $CDCl_3$, 8.20 (s, CH_3), 7.99 (s, CH_3), 7.04 (d, J=5.0 Hz, $NHCH_3$). *Anal.* Calcd. for $C_{12}H_{15}ON$: C,76.15; H, 7.99; N, 7.40. Found: C, 76.44; H, 8.04; N, 7.32.

1-Benzoyl-2-ethylamino-1-propene (Vb), mp 64—65° (from hexane); ν_{max}^{Nujol} 1595, 1535 cm^{-1}. *Anal.* Calcd. for $C_{12}H_{15}ON$: C, 76.15; H, 7.99; N, 7.40. Found: C, 75.65; H, 7.83; N, 7.45.

1-Benzoyl-2-methylamino-1-propene (Vc), mp 71—72° (from hexane); ν_{max}^{Nujol} 1593, 1530 cm^{-1}; τ in $CDCl_3$ 8.04 (s, CH_3), 7.09 (d, J=5.2 Hz, $NHCH_3$), 4.34 (s, –CH=). *Anal.* Calcd. for $C_{11}H_{13}ON$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.31; H, 7.50; N, 8.10.

1-Benzoyl-2-methylamino-1-butene (Vd), mp 59—60° (from hexane); ν_{max}^{Nujol} 1592, 1533 cm^{-1}. *Anal.* Calcd. for $C_{12}H_{15}ON$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.29; H 8.12; N, 7.27.

β-Benzoyl-α-methylaminostyrene (Ve), colorless viscous, ν_{max}^{film} 1570, 1532 cm^{-1}; τ in $CDCl_3$ 7.10 (d, J= 5.2 Hz, $NHCH_3$), 4.23 (s, –CH=). *Anal.* Calcd. for $C_{16}H_{15}ON$: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.00; H, 6.48; N, 5.78.

2-(α-Methylaminoethylidene)-1-tetralone (XII), mp 54—55° (from hexane); ν_{max}^{Nujol} 1590, 1539 cm^{-1}. *Anal.* Calcd. for $C_{13}H_{15}ON$: C, 77.58; H, 7.51; N, 6.96. Found: C, 78.00; H, 7.55; N, 6.89.

Catalytic Reduction of IVa——A mixture of IVa (0.40 g) and Raney Ni (0.5 g) in EtOH (5 ml) was hydrogenated at room temperature under atmospheric pressure. Hydrogenation was stopped when the uptake corresponded to 1.5 mole of H_2 per mole of IVa. Removal of the catalyst and solvent left an oil, which was chromatographed on alumina with C_6H_6. The following products were isolated. α-Ethylidenepropiophenone (VIa), 0.03 g, colorless oil; ν_{max}^{film} 1635 cm^{-1} (C=O); τ in $CDCl_3$ 7.94—8.37 (m, 2-CH_3), 3.61 (qq, J= 6.5, 1.0 Hz, –CH=), 2.50 (m, C_6H_5). *Anal.* Calcd. for $C_{11}H_{12}O$: C, 82.27; H, 7.56. Found: C, 82.46; H, 7.55. It was identified with an authentic sample prepared by the literature method.[7]

α-Ethylpropiophenone (VII), 0.20 g, colorless oil; ν_{max}^{film} 1673 cm^{-1} (C=O); τ 9.00 (t, J=7.0 Hz, CH_3), 8.82 (d, J=7.0 Hz, CH_3), 8.35, 6.63 (m, >$CHCH_2$–), 2.40 (m, C_6H_5). *Anal.* Calcd. for $C_{11}H_{14}O$: C, 81.25; H, 8.71. Found: C, 81.44; H, 8.70. It was identified with a sample obtained by the catalytic reduction of VIa with Pt.

Catalytic Reduction of IVb——A mixture of IVb (0.73 g) and Raney Ni (0.8 g) in EtOH (10 ml) was treated with hydrogen by the similar manner as the above. Isopropylideneacetophenone (VIb), 0.07 g, colorless oil; ν_{max}^{film} 1656 cm^{-1} (C=O); τ in $CDCl_3$ 8.07 (d, J=1.2 Hz, CH_3), 7.82 (d, J=1.2 Hz, CH_3), 3.30 (m, –CH=), 2.37 (m, C_6H_5). *Anal.* Calcd. for $C_{11}H_{12}O$: C, 82.26; H, 7.62. Found: C, 82.46; H, 7.55. It was identified with an authentic sample obtained by the literature method.[8]

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Catalytic Reduction of IVp——A mixture of IVp (0.24 g) and Raney Ni (0.2 g) in EtOH (10 ml) was treated with hydrogen by the similar manner as the above. *o*-(α-Ethylaminophenethyl)phenol (XIV), 0.15 g, colorless oil. *Anal.* Calcd. for $C_{16}H_{19}ON$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.68; H, 7.93; N, 5.32. It was identified with a sample prepared by the following procedure. To a solution of benzylmagnesium chloride in ether (45 ml), prepared from Mg (0.73 g) and benzylchloride (3.8 g) in ether, was added dropwise a solution of salicylaldehyde-ethylimide[23] (1.5 g) in ether (10 ml) with stirring at 3° and the mixture was stirred at 5° for 1 hr. After addition of a solution of NH_4Cl (5 g) in H_2O (40 ml), the mixture was extracted with ether. Evaporation of the solvent left an oil, which was chromatographed on silica gel with $CHCl_3$ to give XIV (0.5 g).

Reaction of N_2H_4–H_2O on Va——A solution of Va (1.06 g), $N_2H_4 \cdot H_2O$ (0.64 g) and HCl (trace) in EtOH (10 ml) was refluxed for 2 hr and then evaporated. After addition of H_2O, the mixture was extracted with ether. Evaporation of the solvent left a colorless viscous, which was distilled to give colorless oil (0.67 g), bp 148° (0.2 mmHg). It was solidified on standing at room temperature. Recrystallization from hexane gave colorless needles (VIIIa), mp 96—98°, which was identified with 3,4-dimethyl-5-phenylpyrazole obtained by the literature method.[9]

Reaction of $N_2H_4 \cdot H_2O$ on Vb——A mixture of Vb (0.12 g), $N_2H_4 \cdot H_2O$ (0.3 g) and HCl (trace) in EtOH (2 ml) was refluxed for 2 hr and then evaporated. The residue was chromatographed on alumina with $CHCl_3$ to give a colorless crystalline solid. Recrystallization from hexane gave colorless needles (VIIIb) (0.08 g), mp 120—122°, which was identified with 3-methyl-5-phenylpyrazole obtained by the literature method.[10]

3-Methyl-4,5-dihydronaphth[2,1-*d*]isoxazole (XIII)——To a solution of XII (6.6 g) in EtOH (7 ml) was added a solution of $NH_2OH \cdot HCl$ (4.6 g) in H_2O (7 ml) with stirring and cooling in an ice bath. The mixture was stirred at room temperature for 3 hr and then refluxed for 1 hr. After removal of EtOH, the residue was extracted with CH_2Cl_2. Evaporation of the solvent left a crystalline solid, which was recrystallized from light petroleum to give colorless prisms (XIII) (5.7 g), mp 58—59°. λ_{max}^{EtOH} 222 nm (log ε 4.16), 228 (4.10), 273 (4.12), 283 (4.16), 294 (4.01), 306 (3.94); τ in $CDCl_3$ 7.74 (s, NCH_3), 7.15 (m, 4H), 2.69 (m, 4H). *Anal.* Calcd. for $C_{12}H_{11}ON$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.75; H, 6.10; N, 7.76.

Thermal-conversion of IV into XV——A solution of IV (5 mmole) in xylene (50 ml) was refluxed for 2.5 hr and then evaporated. The residue was chromatographed on alumina with light petroleum to give XV listed in Table III.

3,4-Diphenyl-1-methylpyrrole (XVa)——To a solution of Na (3.0 g) in MeOH (35 ml) was added a solution of diethyl N-methyliminodiacetate[24] (3.0 g) in MeOH (15 ml) with stirring at room temperature and this was followed by the addition of solid benzil (6.3 g). The mixture was slowly heated to the boiling point, refluxed for 0.5 hr and poured into H_2O (200 ml). After standing overnight under cooling, the mixture was acidified with 2N HCl and the precipitated crystalline solid (1.5 g) was filtered off. This solid (0.27 g) was dissolved in ethanolamine (0.6 ml). After refluxing for 1 hr, the mixture was poured into H_2O. The precipitated crystalline solid was collected by filtration and recrystallized from MeOH to give colorless needles (XVa) (0.21 g), mp 126—127°, which was identical with a sample obtained by the thermal reaction of IVf.

3-Methyl-1-phenyl-3H-benz[*e*]indole (XVIa)——A mixture of XVh (0.3 g) and chloranil (0.3 g) in C_6H_6 (13 ml) was refluxed for 3.5 hr under an atmosphere of nitrogen. Evaporation of the solvent left a crystalline solid, which was chromatographed on alumina with C_6H_6–hexane (1 : 3) to give colorless crystals (0.26 g). Recrystallization from MeOH gave colorless needles (XVIa), mp 114—115°, listed in Tables III and IV.

2,3-Dimethyl-1-phenyl-3H-benz[*e*]indole (XVIb)——A mixture of XVi (0.10 g) and chloranil (0.1 g) in C_6H_6 (3 ml) was treated by the similar manner as the above to give colorless needles (XVIb) (0.07 g), mp 110—111° (see Tables III and IV).

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